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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,488	09/29/2006	Lisa Selsam Beavers	X16949M	9700

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EXAMINER	
ZAREK, PAUL E	
ART UNIT	**PAPER NUMBER**
4161	

NOTIFICATION DATE	DELIVERY MODE
08/25/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/599,488	BEAVERS ET AL.	
	Examiner	Art Unit	
	PAUL ZAREK	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23-26* is/are allowed.

6)☒ Claim(s) *27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-22 have been canceled by the Applicant. Claims 23-27 were added on10/31/2007. Claims 23-27 are currently pending. This is the first Office Action on the merits of the claim(s).

Priority

2. Applicant's claim for the benefit of a prior-filed International Application, PCT/US05/010240 (filed on 03/25/2005) and Provisional Applications, 60/558,542 and 60/617,101 (filed on 04/01/2004 and 10/08/2004, respectively) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date for the Instant Application is 04/01/2004.

Information Disclosure Statement

3. The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which

caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a)

Claim Rejections - 35 USC § 112 (1st paragraph)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue.” (MPEP § 2164.01(a))

a. *The breadth of the claim*: Claim 27 is drawn to a method of treating obesity in a patient in need thereof comprising administering an effective amount of (3-fluoro-4'-methansulfonyl-biphenyl-4-yl)-[2-(2-methyl-pyrrolidin-1-ylmethyl)-pyrrolidin-1-yl]-methanone (the compound claimed in Claim 23). The claimed compound corresponds to X90 (pg 124). Applicant defines "treating obesity" to include preventing obesity (pg 7, lines 20-23);

b. *Nature of the invention*: The nature of the invention is drawn to treating obesity with a histamine H3 receptor antagonist;

c. *The state of the prior art*: The causes of obesity are multifactorial, but with the root cause being more calories consumed than expended. Lifestyle factors play an enormous role in the onset and maintenance of obesity. Limiting caloric intake (i.e. consuming less sugar) and increasing exercise are integral for the effective treatment or prevention of obesity (Dick, Worldviews on Evidence-Based Nursing, 2004, pg 213, "Summary of Findings") Histamine H3 receptor antagonist have been shown to cause weight loss or prevent weight gain (Hancock, et al, Inflammation Research, 2004, pg S47, paragraph 1, lines 5-6);

d. *Level of one of ordinary skill in the art*: Nutritionists, physicians and scientists investigating obesity, weight loss and weight gain represent one of ordinary skill in the art;

e. *Level of predictability in the art*: Reducing the imbalance between caloric intake and expenditure is paramount in treating and preventing obesity. Lifestyle changes are an important facet of any treatment for obesity. de Farranti and Mozaffarian (Clinical

Chemistry, 2008) state that what works for one person does not necessarily work for another. "[T]he optimal methods to implement effective lifestyle changes to reduce obesity on a population level are not well understood." (pg 953, col 1, lines 9-12.). However, pharmaceutical interventions appear to be effective in reducing obesity (pg 951, "Pharmacological Interventions"). Esbenshade, et al., (Molecular Interventions, 2006) teach that histamine H3 receptor antagonists are useful in treating obesity (pg 80, "The H_3 Receptor in Obesity"). Histamine H3 receptor antagonists are extremely diverse in structure, "with structural diversity increasing over time, rather than converging toward any common group of pharmacophores. "(pg 83, col 1, paragraph 3, lines 1-4). Esbenshade et al., speculate that the structural diversity is due, in part, to the "ability of the receptor to accommodate a wide variety of pharmacophores." (pg 83, col 2, lines 1-2) Within this broad class of histamine H3 receptor antagonists, not all appear to be effective in inducing weight loss, and the reasons for this are not currently known (pg 80, col 2, last sentence of section "The H_3 Receptor in Obesity");

f. *Amount of direction provided by the inventor*: Inventor cites that histamine H3 receptor antagonists are an attractive target for the effective treatment of obesity (instant specification, pg 1, lines 29-32 and pg 133, lines 7-10.) Applicant also acknowledges "[a]lthough a number of H3R antagonists are known in the art, none have proven to be satisfactory obesity or cognitive drugs." (pg 133, lines 10-11, emphasis added);

g. *Existence of working examples*: Applicant discloses the Ki of two compounds for the histamine H3 receptor, neither of which are the compound claimed in Claim 1; and,

h. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure*: Dick teaches that lifestyle (i.e. diet and exercise) plays a paramount role in the development of obesity, and that treating obesity requires lifestyle choices that both reduce caloric intake and increase caloric expenditure. de Farranti and Mozaffarian and Esbenshade, et al., teach that pharmacologic interventions can be a useful to the treatment of obesity. However, Esbenshade, et al., also teach that histamine H3 receptor antagonists are extremely structurally diverse and that not all histamine H3 receptor antagonists are equal with respect to anti-obesity activity. Applicant provides no data demonstrating the ability of the claimed compound to antagonize the histamine H3 receptor, nor does the Applicant demonstrate that the claimed compound would be capable of treating obesity. The art suggests that not all histamine H3 receptor antagonists would be effective anti-obesity drugs, and the instant specification does not make up for this deficit. Undue experimentation would be required to use the invention as claimed.

Conclusion

7. Claims 23-26 are currently allowable. A search of the prior art did not reveal the claimed compound or any obvious variants thereof.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL ZAREK whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, PATRICK NOLAN can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Ashwin Mehta/
Primary Examiner, Technology Center 1600